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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,755	10/30/2001	Toshihiro Shimizu	2522 US2P	1478

23115 7590 09/09/2003

TAKEDA PHARMACEUTICALS NORTH AMERICA, INC  
INTELLECTUAL PROPERTY DEPARTMENT  
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LINCOLNSHIRE, IL 60069

EXAMINER

TRAN, SUSAN T

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 09/09/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

10/017,755

Applicant(s)

SHIMIZU ET AL.

Examiner

Susan Tran

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 June 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 1-7,9,11-19,21-29 and 31.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 32,33,36,38-44 and 46-49.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☒ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). 12.
10. ☐ Other: \_\_\_\_\_

**ATTACHMENT**

Receipt is acknowledged of applicant's Supplemental Information Disclosure Statement and Amendment filed 06/02/03.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 32, 33, 36, 38-44, and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu et al. (339), in view of Kamada EP 0 452 862 A2.

Shimizu teaches effervescent composition comprising a core-shell powder surrounding a fine granular core spray-coated with water-soluble polymer, physiologically active substance, and enteric coating layer (see abstract and column 3). The fine granular core having average diameter of about 250  $\mu\text{m}$ , includes crystalline cellulose and 50-70% lactose beads (columns 4-5). The composition further comprises additives, such as, crystalline cellulose, mannitol, lactose, magnesium or calcium carbonate, and mixture thereof (column 6, lines 36-51). The physiologically active substance layer further comprising 0.1 to about 50% low-substituted hydroxypropylcellulose (I-HPC), (see columns 6-7). The amount of active substance is disclosed throughout the examples.

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The examiner notes that Shimizu is silent as to the teaching of the tablet hardness. However, it is the position of the examiner that the particular tablet hardness is inherent since Shimizu is using the same ingredients to obtain the same result desired by the applicant, *i.e.*, tablet dosage form of effervescent fine granules containing acid-labile drug.

Shimizu is relied upon for the reasons stated above. Applicant alleges that Shimizu does not teach a sustained release agent, nor does it identify additives that could be equated to the sustained-release agent of the present invention.

Kamada teaches spherical core being coated with powder layer comprising active ingredients and having an out layer of coating (see abstract). The coating agents can be used alone or in a combination thereof, which includes acrylic polymers, cellulosic polymer, shellac, or the like (page 5, lines 1-14). Thus, it would have been obvious for one of ordinary skill in this art to modify Shimizu's coating agents using the mixture of coating in view of the teaching of Kamada to obtain the claimed invention because the references teach the advantageous results in the use of similar coating agents for acid-labile active drug. The expected result would be effervescent tablet dosage form of fine granules containing acid-labile drug, which will provide accurate controlled release rate.

### ***Response to Arguments***

Applicant's reply has overcome the following rejections: 102(e) rejection by Shimizu '339; 103(a) rejection over Shimizu '339 and Kamada, in view of Shimizu '904.

Applicant's arguments filed 06/02/03 have been fully considered but they are not persuasive.

Applicant argues that Shimizu is not directed to the claimed enteric coating layer. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Moreover, it is noted that Shimizu teaches coating agent can be HPMC, cellulosic polymer, Tween 80, Pluronic, castor oil, *acrylic copolymers (Eudragit®)*, shellac, was, talc, titanium dioxide, *and* red iron oxide (column 7, lines 7-21, and column 9, lines 50-67). Accordingly, such language does suggest a sustained release agent, or additives that could be equated to the sustained-release agent. In the instant case, Shimizu is rejected in view of Kamada.

Applicant argues that Kamada does not cure the deficiencies of Shimizu. Contrary to the applicant's argument, Kamada is relied upon for the teachings of coating agents can be used in a combination of polymers, includes acrylic polymers, cellulosic polymer, shellac, or the like (page 5, lines 1-14). The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Applicant request further clarification of the former rejections under 102(a) and 103(a) by Shimizu '339. It is noted that the Final Office Action dated 03/03/03 had withdrawn these rejections. It is also noted the submission of the five translation of the foreign priority documents had been acknowledged, therefore, the 102(a) rejection was withdrew.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Tran whose telephone number is (703) 306-5816. The examiner can normally be reached from Monday through Thursday from 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 4:30 pm. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

THURMAN K. PAGE, J.D.  
SUPERVISORY PATENT EXAMINER  
